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10/518,103	10/14/2005	Andrei Bugrim		5310

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EXAMINER	
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ART UNIT	PAPER NUMBER
1631	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,103	BUGRIM ET AL.	
	Examiner	Art Unit	
	KARLHEINZ R. SKOWRONEK	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-12* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Status

Claims 1 and 3-12 are pending.

Claim 2 is cancelled.

Claims 1 and 3-12 have been examined.

Claims 1 and 3-12 are rejected.

Priority

The amendment to the specification to perfect the claim to priority is acknowledged.

Specification

Response to Arguments

The objection to the specification to correct embedded hyperlinks and missing US application numbers is withdrawn in view of the amendments to the specification filed 19 May 2008.

Claim Objections

Response to Arguments

Applicant's arguments, see remarks p. 6, filed 19 May 2008, with respect to the objection to claims 1 and 3 have been fully considered. The objection to claims 1 and 3 has been withdrawn in view of the amendments to the claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation." These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to use the claimed invention one of skill in the art must be able to reconstruct metabolic pathways in diseased and non-diseased states involving HC GP-39. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The description describes that there is no direct evidence that HC gp-39 binds heparin p. 11. The specification speculates that HC gp39 has a heparin sulfate than fibronectin (p. 12). The specification indicates that HC gp-39 is expressed by macrophages (p. 14).The specification indicates that HC gp-39 is homologous to DS47

(p. 16) The description does not provide detailed guidance to related to the metabolic pathways in which HC gp-39 function.

c) The description provides working examples of the metabolic reconstruction of amino acid metabolic pathways. The description does not provide working examples of HC gp-39 metabolic pathways.

d) The nature of the invention, metabolic pathway reconstruction, is complex.

e) The prior art does not show any metabolic pathways for HC gp-39. Johansen et al. (Expert Opinion in Therapeutic Targets, Vol. 11, No. 2, p. 219-234, 2007) shows that the exact biological functions of YKL-40 are not known (p. 222, col. 1). Johansen shows membrane receptors mediating the biological effects are not presently known.

f) The skill of those in the art of molecular biology, biochemistry and bioinformatics is high.

g) The predictability of pathways in which HC gp-39 functions in both diseased and non-diseased states to allow reconstruction is unknown in the prior art.

h) The claims are directed to the reconstruction of metabolic pathways in which HC gp-39 functions in both diseased and non-diseased states.

The skilled practitioner would first turn to the instant description for guidance in using the claimed invention. However, the description lacks clear evidence that the metabolic pathways of HC gp-39. As such, the skilled practitioner would turn to the prior art for such guidance, however the prior art does not discuss HC gp-39 and the elucidation of metabolic pathways in which it functions biologically. Finally, said practitioner would turn to trial and error experimentation to determine a relationship

between HC gp-39 and the reconstruction of metabolic pathways in which it functions biologically. Such amounts to undue experimentation.

Claim Rejections - 35 USC § 102

Response to Arguments

Applicant's arguments, see remarks p. 7-8, filed 19 May 2008, with respect to the rejection claim 1 as anticipated over Nakao et al. under 35 USC 102(b) have been fully considered. The rejection of claim 1 has been withdrawn in view of the amendments to the claim.

Claim Rejections - 35 USC § 103

Response to Arguments

Applicant's arguments, see remarks p. 9-10, filed 19 May 2008, with respect to the rejection of claims 1 and 2 as unpatentable over Nakao et al. in view of Okubo et al. under 35 USC 103(a) have been fully considered. The rejection of claims 1 and 2 has been withdrawn in view of the cancellation of claim 2.

Applicant's arguments, see remarks p. 10-12, filed 19 May 2008, with respect to the rejection of claim 3 as unpatentable over Nakao et al. in view of Karp et al. under 35 USC 103(a) have been fully considered. The rejection of claim 3 has been withdrawn in view of the amendments to the claim.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

The following rejection is necessitated by amendment of the claims.

Claims 1, 3-5, and 7-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakao et al. as supported by the KEGG table of contents as of February 1999(online resource, [http://web.archive.org/web/19990203053246/www.genome.ad.jp/kegg/kegg2.html]), in

view of Karp et al. and in view of Kuffner et al. (Bioinformatics, Vol. 16, No. 9, p 825-836, 2000).

The claims are directed to a method for reconstruction the metabolism of an organism in which data regarding the organism metabolism is collected; linked to metabolic pathways; interconnections between metabolic pathways are identified; and a map of the organism's metabolism is created.

Nakao et al. shows a method of metabolism reconstruction. Nakao et al. shows that data regarding the organism's metabolism is collected (sect 3.1). Nakao et al. shows that the data is linked to metabolic pathways and inter connections are identified to create a map of the organism's metabolism (figure 4). Nakao et al. shows that the metabolic reconstruction also comprises data regarding metabolism of an organism for both a reference (non-diseased) and perturbed (diseased) state (p. 95). Although Nakao et al. refers to reference and perturbed states, the KEGG database actually contained data related to diseased and non-diseased states in humans (see the KEGG database table of contents from February 1999) Nakao et al. shows that pathway maps can be reconstructed for eukaryotes such as fruit fly, mouse, human and Saccharomyces cerevisiae.

Nakao et al. does not show the identification of drug targets.

Karp et al. shows that drug targets can be identified through the analysis of pathway genome databases (p. 278, col. 2 to p. 279, col. 1). Karp et al. shows that that integrated genome-metabolic pathways provide a framework for improved drug discovery (abstract).

Kuffner et al. shows a method of that combines the information found on various metabolic databases to produce a differential metabolic display (DMD). The DMD of Kuffner et al. allows the comparison between disease pathways and non-disease pathways (p. 825, col. 2 –p. 825, col. 1). Kuffner et al. suggests differences can be identified from the comparison. Kuffner et al. shows that the data to generate DMD's are taken from such databases as KEGG (p. 826, col. 1). Kuffner et al. shows the type of data obtained from the databases comprises biochemical units further comprising metabolic steps (enzymes), chemical compounds (ligands, cofactors, substrates, and products), reactions, and enzymatic function(genes and proteins) (p. 826, col. 2 and figs1 and 5). Kuffner et al. shows an annotation table comprising fields such as sub cellular localization and intracellular compartmentalization (figure 5). Kuffner et al. suggests that DMD will useful for target identification (abstract). Kuffner et al. shows DMD's allow the display of significant differences, to identify gaps in specific pathways and enable the interpretation of expression data by making predictions for proteins of unknown function and to propose the existence and/or absence of specific proteins or protein functions (p. 834, col. 2).

It would have been obvious to one of skill in the art to modify the method of reconstructing an organism's metabolism of Nakao et al. with the drug target identification of Karp et al. because Karp et al. shows that that integrated genome-metabolic pathways provide a framework for improved drug discovery. It would have been further obvious to modify the method of reconstructing metabolism with collected data of Nakao and the use of pathways to identify targets of Karp et al. with the DMD's

of Kuffner et al. because Kuffner et al. shows DMD's allow the display of significant differences, to identify gaps in specific pathways and enable the interpretation of expression data by making predictions for proteins of unknown function and to propose the existence and/or absence of specific proteins or protein functions.

Claims 1, 3, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakao et al. as supported by the KEGG table of contents as of February 1999(online resource, [http://web.archive.org/web/19990203053246/www.genome.ad.jp/kegg/kegg2.html]), in view of Karp et al. and in view of Kuffner et al. (Bioinformatics, Vol. 16, No. 9, p 825-836, 2000) as applied to claims 1 and 3-5 above, and further in view of Okubo et al. (Nature Genetics, Vol. 2, p. 173-179, November 1992) .

Claim 6 is directed to data that is Expressed sequence tag (EST) data.

Nakao et al. in view of Karp and in view of Kuffner et al. as applied to claims 1 and 3-5 above teach a method of metabolic reconstruction.

Nakao et al. in view of Karp and in view of Kuffner et al. as applied to claims 1 and 3-5 above do not show EST data.

Okubo et al. shows expression data that comprises EST data can be used in mapping (p. 178, col. 1). Okubo shows the advantage of using expressed sequence tags results from a comparison of data from the same cells under different physiological conditions that will aid in the understanding of cell- and time-dependent control of gene

expression (p. 176-177, col. 2). Okubo et al. shows that map of expressed gene will help in the search for biologically and industrially interesting genes (p. 173, col. 1).

It would have been obvious to one of skill in the art to modify the method of metabolism reconstruction of Nakao et al. in view of Karp and in view of Kuffner et al. as applied to claims 1 and 3-5 above with the incorporation of EST data of Okubo et al. because Okubo et al. shows that a map of expressed genes will facilitate the search for biologically and industrially interesting genes.

Claims 1, 3, and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nakao et al. as supported by the KEGG table of contents as of February 1999(online resource, [http://web.archive.org/web/19990203053246/www.genome.ad.jp/kegg/kegg2.html]), in view of Karp et al. and in view of Kuffner et al. (Bioinformatics, Vol. 16, No. 9, p 825-836, 2000) as applied to claims 1 and 3-5 above, and further in view of Kumar (Reactive and Functional Polymers, Vol. 46, p. 1-27, 2000) in view of Tile D4 of the Boerhinger Biochemical pathways map (Roche Applied Science, 1993 Online [http://www.expasy.org/cgi-bin/show_image?D4&up]).

Claim 11 is directed to the at least one pathway comprising a chitinase.

Nakao et al. in view of Karp and in view of Kuffner et al. as applied to claims 1 and 3-5 above teach a method of metabolic reconstruction.

Nakao et al. in view of Karp and in view of Kuffner et al. as applied to claims 1 and 3-5 above do not explicitly show a pathway comprising a chitinase.

Tile D4 of the Boerhinger Biochemical pathways chart shows a biochemical pathway that comprises a chitinase. Tile D4 shows that chitin is degraded by a chitinase to produce chitobiose which is in turn degraded by N-Acetyl-beta-Glucosamidase to produce N-Acetyl-D-Glucosamine. The blue lines as indicated by the legend denote biochemical reactions that occur in animals (p. 4).

Kumar shows that chitin is a functional material of high potential. Kumar shows that the immunogenicity of chitin is exceptionally low (p. 1, col. 1). Kumar shows that chitin is used to dress wounds and as artificial skin (p. 9, col. 2). Kumar shows that wound healing is accelerated by the degradation of the chitin derivative, chitosan (p. 10 col. 1-2).

It would have been obvious to one of skill in the art to modify the method of metabolism reconstruction of Nakao et al. in view of Karp and in view of Kuffner et al. as applied to claims 1 and 3-5 above with a pathway comprising a chitinase as in the tile D4 because Kumar shows the wide range of beneficial applications of chitin. It would have been further obvious to modify the metabolic pathway reconstructions of Nakao et al. in view of Karp and in view of Kuffner et al. as applied to claims 1 and 3-5 above with a pathway comprising tile D4 because the substitution of a metabolic pathway reconstructed to comprise a chitinase for another pathway would have yielded predictable results.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the

unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

This rejection has been amended as necessitated by amendment.

Claims 3, 7 and 8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4 of copending Application No. 11/499, 437. Although the conflicting claims are not identical, they are not patentably distinct from each other because Both claim 3 of the instant application and claim 1 of Application No. 11/499, 437 are directed to the same use, namely to identify drug targets. Claim 1 of Application no. 11/499,437 is alternatively directed to identifying gene therapy targets. Both claim 3 of the instant application and claim 1 of Application No. 11/499, 437 perform the same steps and produce the same result. In addition, claims 7 and 8 of the instant application are directed to further limitation of the data specifically chemical compounds, reading on

metabolite of as recited in claim 4 of Application No. 11/499, 437, and proteins, also as recited in claim 4 of Application No. 11/499, 437.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments, see remarks p. 12, filed 19 May 2008, with respect to the provisional rejection of claim 3 under 35 USC 101 as the same invention have been fully considered. The provisional rejection of claim 3 has been withdrawn in view of the amendments to the claim. However, claim 3 remains provisionally rejected under the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 4 of copending Application No. 11/499, 437.

The following double patenting rejection has been necessitated by amendment.

Claims 1, 3, and 6-8 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-9 of copending Application No. 10/174, 762. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of both applications are drawn to the reconstruction of metabolic pathways of an organism. Both methods rely on the collection of data regarding an organism's metabolism; linking the data into metabolic pathways and identifying interconnections between metabolic pathways. Both methods also have embodiments in which the data is expressed sequence tag data and heterogeneous.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to KARLHEINZ R. SKOWRONEK whose telephone number is (571) 272-9047. The examiner can normally be reached on 8:00am-5:00pm Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/K. R. S./
Examiner, Art Unit 1631

19 August 2008
/John S. Brusca/
Primary Examiner, Art Unit 1631